

Amendments to the Specification:

Please replace paragraph [0008] with the following paragraph:

[0008] As a result, what is needed is a simple propofol formulation for the production of high concentrations of propofol in a completely transparent microemulsion that can be used as an intravenously administered anesthetic, and if necessary can be suitably colored in order to identify different concentrations of propofol in different preparations. In addition, there is needed a propofol self-microemulsifiable ~~microemulsifiable~~ base composition which uses only a single hydrophilic surfactant, is easy to sterilize, can be stored indefinitely until the anesthetic is needed, after which it can easily be reconstituted by addition of a physiologic saline or similar water-based carrier. The present invention satisfies these needs, among others.

Please replace paragraph [0009] with the following paragraph:

[0009] The present invention generally provides a novel method and a composition for enhancing the dissolution and bioavailable properties of propofol (2, 6 diisopropyl phenol) for use as an intravenously administered anesthetic in mammals. The method of the present invention produces a self-microemulsifiable~~microemulsifiable~~ emulsion base composition that is utilized in the production of a water-based microemulsion preparation for use as an anesthetic. In a preferred two (2) component base composition, the base composition consists of: a surfactant, containing polyethylene glycol; and liquid propofol. The microemulsion is prepared by mixing the base composition with a carrier liquid, which results in the formation of a microemulsion containing concentrations of propofol of up to about 4% by weight of propofol to the volume of the microemulsion. In a four (4) component base composition, the base composition consists of: a surfactant, containing polyethylene glycol; liquid propofol; a water-immiscible solvent; and ethanol. The microemulsion is prepared by mixing the base composition with a carrier liquid, which results in the formation of a microemulsion containing concentrations of propofol of up to about 10% by weight of propofol to the

volume of the microemulsion. The present invention produces a base composition that is a self-~~microemulsifiable~~microemulsifiable, anhydrous, homogenous, and optically transparent liquid that can be stored for later use almost indefinitely. As a result, the preparation of the propofol microemulsion by mixing the base composition with the carrier liquid can be delayed until the anesthetic is needed in the laboratory, clinic or hospital. Further, the present invention produces a microemulsion which is thermodynamically stable and is also optically transparent. The transparency of the microemulsion permits the anesthetic to be tinted with different colors in order to distinguish different propofol concentrations, so that accidents involving anesthetics of similar appearance, but containing different concentrations of propofol, are more easily avoided. The transparency of the microemulsion also makes it easier to detect whether the anesthetic has been contaminated. The microemulsion of the present invention is also easily sterilized by simply heating the surfactant before it is mixed with the liquid propofol and by using a sterilized carrier liquid. The characteristics of the invention are also extremely conducive to cold filtration filter sterilization.

Please replace paragraph [0010] with the following paragraph:

[0010] The present invention generally provides a novel method and a composition for enhancing the dissolution and bioavailable properties of propofol (2, 6 diisopropyl phenol) for use as an intravenously administered anesthetic in mammals. The method of the present invention produces a self-~~microemulsifiable~~microemulsifiable emulsion base composition that is utilized in the production of a water-based microemulsion preparation for use as an anesthetic. In a preferred two (2) component base composition, the microemulsion preparation contains concentrations of propofol of up to about 4% by weight of propofol to the volume of the microemulsion, and in a four (4) component base composition, the microemulsion preparation contains concentrations of propofol of up to about 10% by weight of propofol to the volume of the microemulsion.

Please replace paragraph [0012] with the following paragraph:

[0012] The preferred method of producing the self-~~microemulsifiable~~~~microemulsifiable~~ emulsion base composition consists essentially of mixing a predetermined amount of the PEG-containing surfactant, preferably heated to a preparation temperature above its melting point, with a predetermined amount of the liquid propofol. The mixing is ~~performed~~~~performed~~ by simply stirring or agitating the components for a few minutes or less until the solution becomes transparent. The resulting base composition is a self-~~microemulsifiable~~~~microemulsifiable~~, anhydrous, homogenous, and optically transparent liquid, with low viscosity at the preparation temperature. The water-based microemulsion is then prepared by mixing the base composition with a predetermined amount of a carrier liquid, which contains water and is isotonic to blood, such as 0.9% saline, 5% dextrose, or other isotonic solutions containing a crystalloid or a colloid which are intended for peripheral intravenous administration. Again, the mixing is ~~performed~~~~performed~~ by simply stirring or agitating the components for a few minutes or less until the solution becomes transparent. The resulting microemulsion preparation may contain concentrations of propofol of up to about 4% by weight of the propofol to the volume of the microemulsion (w/v), and still exhibit all of the characteristics of a microemulsion. The microemulsion is thermodynamically stable at room temperature and is optically transparent, but has a pale yellow color due to the inclusion of propofol. Examples #1 and #2 at the end of this section set forth specific examples of the preparation of a two (2) component base composition and then using the base to prepare a microemulsion containing concentrations of propofol of 1% (w/v) and 4% (w/v), respectively. Example #3 sets forth the results of the intravenous administration of the microemulsion containing a concentration of propofol of 4%, prepared as in Example #2, to a canine, without any evidence of pain upon intravenous injection to the conscious animal.

Please replace paragraph [0019] with the following paragraph:

[0019] Another feature of the present invention is that the self-~~microemulsifiable~~microemulsifiable emulsion base composition may be stored in an air tight vial, ampoule, or other similar container almost indefinitely. As a result, the preparation of the propofol microemulsion, by mixing the base composition with a carrier liquid, can be delayed until the aesthetic is needed in the laboratory, clinic or hospital. Although the preferred base composition will solidify after it cools to room temperature, the base can be easily returned to its liquid state by warming the base to a temperature of approximately 45° C. Then the microemulsion liquid preparation is readily formed by mixing the liquid base with the carrier liquid. This feature greatly enhances the usefulness and convenience of microemulsions prepared in accordance with the method of the present invention. Current oil-in-water type microemulsions containing the anesthetic propofol cannot be prepared in similar fashion because they are not thermodynamically stable, and require technologically sophisticated emulsification preparation, analogous to homogenization of milk. This cannot be done in the field or at the bedside.

Please replace paragraph [0020] with the following paragraph:

[0020] The self-~~microemulsifiable~~microemulsifiable emulsion base composition of the present invention includes a PEG-containing surfactant that is completely miscible with water, meaning that the PEG-containing surfactant has a high affinity for water and readily dissolves in water, where the surfactant forms an optically clear so-called "micellar solution" (i.e., not a true chemical solution, but rather an apparent solution in which the surfactant actually consists of aggregates, which are essentially microemulsion particles which lack chemically distinct cores). In a less polar solvent such as ethanol, these classes of surfactants do form true chemical solutions. It is this characteristic of forming a spontaneous micellar solution in water that causes the solubilized composition of propofol and this class of surfactant to form a micellar microemulsion in the water-based carrier liquid.

Please replace paragraph [0032] with the following paragraph:

[0032] In this embodiment the preferred method of producing the self-~~microemulsifiable~~~~microemulsifyable~~ emulsion base composition consists essentially of mixing in any order a predetermined amount of the PEG-containing surfactant, preferably heated to a preparation temperature above its melting point, with predetermined amounts of the liquid propofol, water-immiscible solvent, and ethanol as a co-solvent. The mixing is ~~performed~~~~performed~~ by simply stirring or agitating the components for a few minutes or less until the solution becomes transparent. The resulting base composition is a self-~~microemulsifiable~~~~microemulsifyable~~, anhydrous, homogenous, and optically transparent liquid, with low viscosity at the preparation temperature. The water-based microemulsion is then prepared at room temperature by mixing the base composition with a predetermined amount of carrier liquid, which contains water and is isotonic to blood, such as 0.9% saline, 5% dextrose, or other isotonic solutions containing a crystalloid or a colloid which are intended for intravenous administration. Again, the mixing is ~~performed~~~~performed~~ by simply stirring or agitating the components for a few minutes or less until the solution becomes transparent. The resulting microemulsion preparation can contain concentrations of propofol of up to about 10% by weight of the propofol to the volume of the preparation and still exhibit the characteristics of a microemulsion. The microemulsion is thermodynamically stable at room temperature and is optically transparent, but has a pale yellow color due to the inclusion of propofol. Examples #4, #6, and #7 at the end of this section set forth specific examples of this embodiment in the preparation of a self-~~microemulsifiable~~~~microemulsifyable~~ emulsion base composition and then using the base to prepare a microemulsion containing concentrations of propofol of about 1% (w/v) and up to about 10% (w/v). Example #5 sets forth the results of the administration of a microemulsion containing a concentration of propofol of 10%, prepared as in Example #4, to a canine. Example #8 sets forth the results of the administration of a microemulsion containing a concentration of propofol of 1%, prepared as in Example #7, to a canine.